--35. A method of treating polycystic kidney disease comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.--

Amend Claims 1, 6, 22 and 24-27 as follows:

## 1. A compound having the formula:

wherein,

B2

Each R<sup>1</sup> and R<sup>2</sup> is independently R<sup>3</sup>; R<sup>8</sup>; NHR<sup>3</sup>; NHR<sup>5</sup>; NHR<sup>6</sup>; NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>R<sup>6</sup>; heterocyclyl optionally substituted with 1-4 independent R<sup>4</sup> on each ring; or C1-C10 alkyl substituted with 1-4 independent R<sup>4</sup>;

Each  $R^3$  is independently aryl; phenyl optionally substituted with 1-5 independent  $R^4$  on each ring; or heteroaryl optionally substituted with 1-4 independent  $R^4$  on each ring;

Each n is independently 1 or 2;

Each m is independently 0, 1, 2, 3, or 4;

Each  $R^4$  is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl;  $R^8$ ; halo; haloalkyl;  $SR^5$ ;  $OR^5$ ;  $OC(O)R^5$ ;  $NR^5R^5$ ;  $NR^5R^6$ ;  $NR^5R^{16}$ ;  $COOR^5$ ;  $NO_2$ ; CN;  $C(O)R^5$ ;  $C(O)C(O)R^5$ ;  $C(O)NR^5R^5$ ;  $S(O)_nR^5R^5$ ;  $NR^5C(O)NR^5R^5$ ;  $NR^5C(O)C(O)R^5$ ;  $NR^5C(O)R^5$ ;  $NR^5C(O)C(O)NR^5R^5$ ;  $NR^5C(O)R^5$ ;  $NR^5C(O)C(O)NR^5R^5$ ;  $NR^5C(O)R^5$ ;  $NR^5$ 

Each R<sup>5</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R<sup>9</sup>; haloalkyl; C1-C10 alkyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>9</sup> groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>9</sup>;

B2

Each  $R^6$  is independently  $C(O)R^5$ ,  $COOR^5$ ,  $C(O)NR^5R^5$ ,  $C(=N R^5) NR^5R^5$ , or  $S(O)_n R^5$ ;

Each  $R^7$  is independently halo,  $CF_3$ ,  $SR^{10}$ ,  $OR^{10}$ ,  $OC(O)R^{10}$ ,  $NR^{10}R^{10}$ ,  $NR^{10}R^{11}$ ,  $NR^{11}R^{11}$ ,  $COOR^{10}$ ,  $NO_2$ , CN,  $C(O)R^{10}$ ,  $OC(O)NR^{10}R^{10}$ ,  $C(O)NR^{10}R^{10}$ ,  $N(R^{10})C(O)R^{10}$ ,  $N(R^{10})C(O)$ 

Each R<sup>8</sup> is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R<sup>9</sup>; halo; sulfur; oxygen; CF<sub>3</sub>; SR<sup>5</sup>; OR<sup>5</sup>; OC(O)R<sup>5</sup>; NR<sup>5</sup>R<sup>5</sup>; NR<sup>6</sup>R<sup>6</sup>; NR<sup>6</sup>R<sup>6</sup>; COOR<sup>5</sup>; NO<sub>2</sub>; CN; C(O)R<sup>5</sup>; C(O)NR<sup>5</sup>R<sup>5</sup>; S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>9</sup>; NR<sup>5</sup>S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>R<sup>9</sup>; C1-C10 alkyl substituted with 1-3 independent R<sup>7</sup>, R<sup>9</sup> or aryl;

Each R<sup>9</sup> is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF<sub>3</sub>; haloalkyl; SR<sup>10</sup>; OR<sup>10</sup>; NR<sup>10</sup>R<sup>10</sup>; NR<sup>10</sup>R<sup>11</sup>; NR<sup>11</sup>R<sup>11</sup>; COOR<sup>10</sup>; NO<sub>2</sub>; CN; C(O)R<sup>10</sup>; S(O)<sub>n</sub>R<sup>10</sup>; S(O)<sub>n</sub>NR<sup>10</sup>R<sup>10</sup>; or C(O)NR<sup>10</sup>R<sup>10</sup>;

Each  $R^{10}$  is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo,  $OR^{12}$ ,  $SR^{12}$ ,  $NR^{12}R^{12}$ ,  $COOR^{12}$ ,  $NO_2$ , CN,  $C(O)R^{12}$ ,  $C(O)R^{12}R^{12}$ ,  $NR^{12}C(O)R^{12}$ ,  $N(R^{12})(COOR^{12})$ ,  $S(O)_nNR^{12}R^{12}$ , or  $OC(O)R^{12}$ ; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo,  $CF_3$ ,  $OR^{12}$ ,  $SR^{12}$ ,  $NR^{12}R^{12}$ ,  $COOR^{12}$ ,  $NO_2$ , CN,  $C(O)R^{12}$ ,  $C(O)NR^{12}R^{12}$ ,  $NR^{12}C(O)R^{12}$ ,  $N(R^{12})(COOR^{12})$ ,  $S(O)_nNR^{12}R^{12}$ , or  $OC(O)R^{12}$ ;

Each  $R^{11}$  is independently  $C(O)R^{10}$ ,  $COOR^{10}$ ,  $C(O)NR^{10}R^{10}$  or  $S(O)_nR^{10}$ ;

Each R<sup>12</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF<sub>3</sub>, OR<sup>13</sup>, SR<sup>13</sup>, NR<sup>13</sup>R<sup>13</sup>, COOR<sup>13</sup>, NO<sub>2</sub>, CN, C(O)R<sup>13</sup>, C(O)NR<sup>13</sup>R<sup>13</sup>, NR<sup>13</sup>C(O)R<sup>13</sup>, or OC(O)R<sup>13</sup>; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF<sub>3</sub>, OR<sup>13</sup>, SR<sup>13</sup>, NR<sup>13</sup>R<sup>13</sup>, COOR<sup>13</sup>, NO<sub>2</sub>, CN, C(O)R<sup>13</sup>, C(O)NR<sup>13</sup>R<sup>13</sup>, NR<sup>13</sup>C(O)R<sup>13</sup>, or OC(O)R<sup>13</sup>;

Each R<sup>13</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR<sup>14</sup>, SR<sup>14</sup>, NR<sup>14</sup>R<sup>14</sup>, COOR<sup>14</sup>, NO<sub>2</sub>, CN; or phenyl optionally substituted with halo, CF<sub>3</sub>, OR<sup>14</sup>, SR<sup>14</sup>, NR<sup>14</sup>R<sup>14</sup>, COOR<sup>14</sup>, NO<sub>2</sub>, CN;

Each  $R^{14}$  is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl; Each  $R^{16}$  is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl;  $R^8$ ; halo; haloalkyl; COOR<sup>5</sup>; C(O)R<sup>5</sup>; C(O)R<sup>5</sup>; C(O)R<sup>5</sup>; S(O)<sub>n</sub>R<sup>5</sup>: S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; C1-C10 alkyl substituted with 1-3 independent aryl,  $R^7$ ,  $R^8$ , or phenyl optionally substituted with substituted with 1-4 independent  $R^{23}$ ; or C2-C10 alkenyl substituted with 1-3 independent aryl,  $R^7$  or  $R^8$ ;

Each  $R^{23}$  is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl;  $R^8$ ; halo; haloalkyl;  $SR^5$ ;  $OR^5$ ;  $OC(O)R^5$ ;  $NR^5R^5$ ;  $NR^5R^6$ ;  $COOR^5$ ;  $NO_2$ ; CN;  $C(O)R^5$ ;  $C(O)C(O)R^5$ ;  $C(O)NR^5R^5$ ;  $C(O)NR^5$ ;  $C(O)NR^$ 

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, including perhaloalkyl;

Each aryl is independently a 6-carbon monocyclic, 10-carbon bicyclic or 14-carbon tricyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R<sup>9</sup>; halo; haloalkyl; OR<sup>10</sup>; SR<sup>10</sup>; NR<sup>10</sup>R<sup>10</sup>; NR<sup>10</sup>R<sup>11</sup>; COOR<sup>10</sup>; NO<sub>2</sub>; CN; C(O)R<sup>10</sup>; C(O)C(O)R<sup>10</sup>; C(O)NR<sup>10</sup>R<sup>10</sup>; N(R<sup>10</sup>)C(O)NR<sup>10</sup>R<sup>10</sup>; N(R<sup>10</sup>)C(O)R<sup>10</sup>; N(R<sup>10</sup>)C(O)R<sup>10</sup>; N(R<sup>10</sup>)C(O)C(O)R<sup>10</sup>;

 $NR^{10}C(O)R^9; NR^{10}S(O)_nNR^{10}R^{10}; NR^{10}S(O)_nR^9; NR^{12}C(O)C(O)NR^{12}R^{12}; S(O)_nR^{10}; \\ S(O)_nNR^{10}R^{10}; OC(O)R^{10}; C1-C10 \ alkyl \ substituted \ with 1-3 \ independent \ R^9, halo, CF_3, OR^{10}, \\ SR^{10}, OC(O)R^{10}, NR^{11}R^{11}, NR^{10}R^{10}, NR^{10}R^{11}, COOR^{10}, NO_2, CN, C(O)R^{10}, OC(O)NR^{10}R^{10}, \\ C(O)NR^{10}R^{10}, N(R^{10})C(O)R^{10}, N(R^{10}) \ (COOR^{10}), S(O)_nNR^{10}R^{10}; R^{10}; or \ C2-C10 \ alkenyl \\ substituted \ with 1-3 \ independent \ R^9, halo, CF_3, OR^{10}, SR^{10}, OC(O)R^{10}, NR^{11}R^{11}, NR^{10}R^{10}, \\ NR^{10}R^{11}, COOR^{10}, NO_2, CN, C(O)R^{10}, OC(O)NR^{10}R^{10}, C(O)NR^{10}R^{10}, N(R^{10})C(O)R^{10}, N(R^{10}) \\ (COOR^{10}), S(O)_nNR^{10}R^{10}; \\ \\$ 

Each heterocyclyl is independently a 3-8 membered nonaromatic monocyclic, 8-12 membered nonaromatic bicyclic, or 11-14 membered nonaromatic tricyclic, ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

Each heteroaryl is independently a 5-8 membered aromatic monocyclic, 8-12 membered aromatic bicyclic, or 11-14 membered aromatic tricyclic ring system having 1-4 heteroatoms if monocyclic, 1-8 heteroatoms if bicyclic, or 1-10 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S;

provided  $R^1$  and  $R^2$  are not both 1-alkylpyridinium, <u>or</u> both 4-pyridyl; further provided neither  $R^1$  or  $R^2$  is morpholino or  $NH_2$ ;

6. The compound of claim 1 wherein,

R<sup>1</sup> is independently NHR<sup>5</sup>;

R<sup>2</sup> is independently NHR<sup>3</sup>;

Each  $R^3$  is independently aryl; phenyl optionally substituted with 1-5 independent  $R^4$  on each ring; or heteroaryl optionally substituted with 1-4 independent  $R^4$  on each ring;

Each R<sup>4</sup> is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R<sup>8</sup>; halo; CF<sub>3</sub>; SR<sup>5</sup>; OR<sup>5</sup>; OC(O)R<sup>5</sup>; NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>R<sup>6</sup>; NR<sup>5</sup>R<sup>16</sup>; COOR<sup>5</sup>; NO<sub>2</sub>; CN; C(O)R<sup>5</sup>; C(O)C(O)R<sup>5</sup>; C(O)NR<sup>5</sup>R<sup>5</sup>; S(O)<sub>n</sub>R<sup>5</sup>: S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>8</sup>; NR<sup>5</sup>S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>R<sup>8</sup>; NR<sup>5</sup>C(O)C(O)NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)C(O)NR<sup>5</sup>R<sup>6</sup>; OC(O)NR<sup>5</sup>R<sup>5</sup>; OS(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>OR<sup>5</sup>; P(O)(OR<sup>5</sup>)<sub>2</sub>; C1-C10 alkyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>8</sup>; or C2-C10 alkenyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>8</sup>;

B3

Each R<sup>5</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R<sup>9</sup>; haloalkyl; C1-C10 alkyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>9</sup> groups; C3-C10 cycloalkyl substituted with 1-3 independent aryl, R<sup>7</sup> or R<sup>9</sup>;

Each  $R^6$  is independently  $C(O)R^5$ ,  $COOR^5$ ,  $C(O)NR^5R^5$ ,  $C(=NR^5)NR^5R^5$ , or  $S(O)_n$   $R^5$ ;

Each  $R^7$  is independently halo,  $CF_3$ ,  $SR^{10}$ ,  $OR^{10}$ ,  $OC(O)R^{10}$ ,  $NR^{10}R^{10}$ ,  $NR^{10}R^{11}$ ,  $NR^{11}R^{11}$ ,  $COOR^{10}$ ,  $NO_2$ , CN,  $C(O)R^{10}$ ,  $OC(O)NR^{10}R^{10}$ ,  $C(O)NR^{10}R^{10}$ ,  $N(R^{10})C(O)R^{10}$ ,  $N(R^{10})$  ( $COOR^{10}$ ),  $S(O)_nNR^{10}R^{10}$ ;  $NR^{10}S(O)_nNR^{10}R^{10}$ ;  $NR^{10}S(O)_nR^{10}$ ; or  $P(O)(OR^5)_2$ ;

Each R<sup>8</sup> is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2, 3 or 4 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R<sup>9</sup>; halo; sulfur; oxygen; CF<sub>3</sub>; SR<sup>5</sup>; OR<sup>5</sup>; OC(O)R<sup>5</sup>; NR<sup>5</sup>R<sup>5</sup>; NR<sup>6</sup>R<sup>6</sup>; NR<sup>6</sup>R<sup>6</sup>; COOR<sup>5</sup>; NO<sub>2</sub>; CN; C(O)R<sup>5</sup>; C(O)NR<sup>5</sup>R<sup>5</sup>; S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>9</sup>; NR<sup>5</sup>S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>R<sup>9</sup>; C1-C10 alkyl substituted with 1-3 independent R<sup>7</sup>, R<sup>9</sup> or aryl; or C2-C10 alkenyl substituted with 1-3 independent R<sup>7</sup>, R<sup>9</sup> or aryl;

Each R<sup>9</sup> is independently a 3-8 membered monocyclic, 7-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms independently selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF<sub>3</sub>; haloalkyl; SR<sup>10</sup>; OR<sup>10</sup>; NR<sup>10</sup>R<sup>10</sup>; NR<sup>10</sup>R<sup>11</sup>; NR<sup>11</sup>R<sup>11</sup>; COOR<sup>10</sup>; NO<sub>2</sub>; CN; C(O)R<sup>10</sup>; S(O)<sub>n</sub>R<sup>10</sup>; S(O)<sub>n</sub>NR<sup>10</sup>R<sup>10</sup>; or C(O)NR<sup>10</sup>R<sup>10</sup>:

Each R<sup>10</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, OR<sup>12</sup>, SR<sup>12</sup>, NR<sup>12</sup>R<sup>12</sup>, COOR<sup>12</sup>, NO<sub>2</sub>, CN, C(O)R<sup>12</sup>, C(O)NR<sup>12</sup>R<sup>12</sup>, NR<sup>12</sup>C(O)R<sup>12</sup>, N(R<sup>12</sup>)(COOR<sup>12</sup>), S(O)<sub>n</sub>NR<sup>12</sup>R<sup>12</sup>, or OC(O)R<sup>12</sup>; or phenyl optionally substituted with 1-3

$$\label{eq:condition} \begin{split} &\text{independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10}\\ &\text{cycloalkenyl, halo, CF_3, OR^{12}, SR^{12}, NR^{12}R^{12}, COOR^{12}, NO_2, CN, C(O)R^{12}, C(O)NR^{12}R^{12},\\ &NR^{12}C(O)R^{12}, N(R^{12})(COOR^{12}), S(O)_nNR^{12}R^{12}, \text{ or OC(O)R}^{12}; \end{split}$$

Each  $R^{11}$  is independently  $C(O)R^{10}$ ,  $COOR^{10}$ ,  $C(O)NR^{10}R^{10}$  or  $S(O)_nR^{10}$ ;

Each R<sup>12</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl substituted with 1-3 independent C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF<sub>3</sub>, OR<sup>13</sup>, SR<sup>13</sup>, NR<sup>13</sup>R<sup>13</sup>, COOR<sup>13</sup>, NO<sub>2</sub>, CN, C(O)R<sup>13</sup>, C(O)NR<sup>13</sup>R<sup>13</sup>, NR<sup>13</sup>C(O)R<sup>13</sup>, or OC(O)R<sup>13</sup>; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF<sub>3</sub>, OR<sup>13</sup>, SR<sup>13</sup>, NR<sup>13</sup>R<sup>13</sup>, COOR<sup>13</sup>, NO<sub>2</sub>, CN, C(O)R<sup>13</sup>, C(O)NR<sup>13</sup>R<sup>13</sup>, NR<sup>13</sup>C(O)R<sup>13</sup>, or OC(O)R<sup>13</sup>;

Each R<sup>13</sup> is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, OR<sup>14</sup>, SR<sup>14</sup>, NR<sup>14</sup>R<sup>14</sup>, COOR<sup>14</sup>, NO<sub>2</sub>, CN; or phenyl optionally substituted with halo, CF<sub>3</sub>, OR<sup>14</sup>, SR<sup>14</sup>, NR<sup>14</sup>R<sup>14</sup>, COOR<sup>14</sup>, NO<sub>2</sub>, CN;

Each R<sup>14</sup> is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each  $R^{16}$  is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl;  $R^8$ ; halo; CF<sub>3</sub>; COOR<sup>5</sup>; C(O)R<sup>5</sup>; C(O)C(O)R<sup>5</sup>; C(O)NR<sup>5</sup>R<sup>5</sup>; S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; C1-C10 alkyl substituted with 1-3 independent aryl,  $R^7$ ,  $R^8$ , or phenyl optionally substituted with substituted with 1-4 independent  $R^{23}$ ; or C2-C10 alkenyl substituted with 1-3 independent aryl,  $R^7$  or  $R^8$ ; and

Each  $R^{23}$  is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl;  $R^8$ ; halo; CF<sub>3</sub>; SR<sup>5</sup>; OR<sup>5</sup>; OC(O)R<sup>5</sup>; NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>R<sup>6</sup>; COOR<sup>5</sup>; NO<sub>2</sub>; CN; C(O)R<sup>5</sup>; C(O)C(O)R<sup>5</sup>; C(O)NR<sup>5</sup>R<sup>5</sup>; S(O)<sub>n</sub>R<sup>5</sup>· S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>5</sup>; NR<sup>5</sup>C(O)R<sup>8</sup>; NR<sup>5</sup>S(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>R<sup>8</sup>; NR<sup>5</sup>S(O)<sub>n</sub>R<sup>8</sup>; NR<sup>5</sup>C(O)C(O)NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>C(O)C(O)NR<sup>5</sup>R<sup>5</sup>; OC(O)NR<sup>5</sup>R<sup>5</sup>; OS(O)<sub>n</sub>NR<sup>5</sup>R<sup>5</sup>; NR<sup>5</sup>S(O)<sub>n</sub>OR<sup>5</sup>; P(O)(OR<sup>5</sup>)<sub>2</sub>; C1-C10 alkyl substituted with 1-3 independent aryl,  $R^7$  or  $R^8$ ; or C2-C10 alkenyl substituted with 1-3 independent aryl,  $R^7$  or  $R^8$ ;

provided neither R<sup>1</sup> nor R<sup>2</sup> is NH<sub>2</sub>.



- 22. A composition comprising a compound of any of claims 1-7 and 10-21 and a pharmaceutically acceptable carrier.
  - 24. A method of treating kinase-mediated disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.
  - 25. A method of inhibiting kinase activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.
  - 26. A method of treating disease or disease symptoms in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.
  - 27. A method of inhibiting angiogenesis or vasculogenesis activity in a mammal comprising administration of a composition comprising an effective amount of a compound of any of claims 1-7 and 10-21.